RECOMBINANT BACTERIAL SYSTEM WITH ENVIRONMENTALLY LIMITED VIABILITY

Abstract of the Invention

Disclosed is an Environmentally Limited Viability System (ELVS) for microorganisms based on differences between permissive and non-permissive environments. Viability of the microorganisms are limited to a permissive environment by specifically expressing one or more essential genes only in the permissive environment, and/or expressing one or more lethal genes only in the non-permissive environment. Temporary viability in a non-permissive environment can be achieved by temporarily expressing one or more essential genes in a non-permissive environment, and/or temporarily delaying expression of one or more lethal genes in the non-permissive environment. Environmentally Limited Viability Systems are also disclosed involving coordinate expression of a combination of essential genes and lethal genes. Microorganisms containing an Environmentally Limited Viability System are useful for release into permissive and non-permissive environments. Temperature regulated Environmentally Limited Viability Systems and delayed death Environmentally Limited Viability Systems are particularly suited for delivery of expression products, such as antigens, using recombinant avirulent Salmonella by limiting their growth to the warmer environment inside the host, or by allowing growth for only a limited time in the host.